



## Who Will Develop Epilepsy Following Hospital Discharge? Think Again

### Long-Term Risk of Seizures in Adult Survivors of Sepsis.

Reznik ME, Merkler AE, Mahta A, Murthy SB, Claassen J, Kamel H. *Neurology* 2017;89:1476–1482.

**OBJECTIVE:** To examine the association between sepsis and the long-term risk of seizures. **METHODS:** We conducted a retrospective population-based cohort study using administrative claims data from all emergency department visits and hospitalizations at nonfederal acute care hospitals in California, Florida, and New York from 2005 to 2013. Using previously validated diagnosis codes, we identified all adult patients hospitalized with sepsis. Our outcome was any emergency department visit or hospitalization for seizure. Poisson regression and demographic data were used to calculate age-, sex-, and race-standardized incidence rate ratios (IRR). To confirm our findings, we used a matched cohort of hospitalized patients without sepsis for comparison and additionally assessed claims data from a nationally representative 5% sample of Medicare beneficiaries. **RESULTS:** We identified 842,735 patients with sepsis. The annual incidence of seizure was 1.29% (95% confidence interval [CI] 1.27%–1.30%) in patients with sepsis vs 0.16% (95% CI 0.16%–0.16%) in the general population (IRR 4.98; 95% CI 4.92–5.04). A secondary analysis using matched hospitalized patients confirmed these findings (IRR 4.33; 95% CI 4.13–4.55), as did a separate analysis of Medicare beneficiaries, in whom we found a similar strength of association (IRR 2.72; 95% CI 2.60–2.83), as we did in patients  $\geq 65$  years of age in our primary statewide data (IRR 2.83; 95% CI 2.78–2.88). **CONCLUSIONS:** We found that survivors of sepsis faced a significantly higher long-term risk of seizures than both the general population and other hospitalized patients. Our findings suggest that sepsis is associated with pathways that lead to permanent neurologic sequelae.

### Post-stroke Seizures Are Clinically Underestimated.

Bentes C, Martins H, Peralta AR, Casimiro C, Morgado C, Franco AC, Fonseca AC, Galdes R, Canhão P, Pinho E Melo T, Paiva T, Ferro JM. *J Neurol* 2017;264:1978–1985.

Cerebrovascular disease is the leading cause of epilepsy in adults, although post-stroke seizures reported frequency is variable and few studies used EEG in their identification. To describe and compare EEG and clinical epileptic manifestations frequency in patients with an anterior circulation ischaemic stroke. Prospective study of acute anterior circulation ischemic stroke patients, consecutively admitted to a Stroke Unit over 24 months and followed-up for 1 year. All patients underwent standardized clinical and diagnostic assessment. Seizure occurrence was clinically evaluated during hospitalization and by a telephone interview at 6 months and a clinical appointment at 12 months after stroke. Video-EEG was performed in the first 72 h (1st EEG), daily after the 1st EEG for the first 7 days after the stroke, or later if neurological worsening, at discharge, and at 12 months. 151 patients were included (112 men) with a mean age of 67.4 (11.9) years. In the 1st year after stroke, 38 patients (25.2%) had an epileptic seizure. During hospitalization, 27 patients (17.9%) had epileptiform activity (interictal or ictal) in the EEG, 7 (25.9%) of them electrographic seizures. During the first week after stroke, 22 (14.6%) patients had a seizure and 4 (2.6%) nonconvulsive status epilepticus criteria. Five (22.7%) acute symptomatic seizures were exclusively electrographic. At least one remote symptomatic seizure occurred in 23 (16%) patients. In the first 7 days after stroke, more than one-fifth of patients with seizures had exclusively electrographic seizures. Without a systematic neurophysiological evaluation the frequency of post-stroke seizures are clinically underestimated.



## Commentary

Thanks to the contribution of continuous video EEG monitoring in the hospital setting, it is clear by now that a significant portion of patients in the medical and neurologic intensive care units have active nonconvulsive or purely electrographic seizures during the acute phase of their illness (1). These seizures, while nonconvulsive in many instances, do have clinical manifestations as they contribute to focal deficits or altered mental status, which may be treatable and reversible.

We know less, however, of the long-term impact of these conditions in the development of chronic epilepsy and its manifestations or the impact of unrecognized (and untreated) seizures on functional recovery after an acute stroke or intensive care stay. It is also unclear which of these patients need long-term antiseizure medication treatment or what proportion of them will develop epilepsy.

The elderly population is particularly vulnerable to developing new-onset epilepsy after a stroke or acute illness. They are also known to develop seizures, which are difficult to identify as they may have only subtle clinical manifestations (2). Stroke and sepsis pose an increased risk for long-term epilepsy to an extent that deserves higher awareness and, potentially, a discussion with patients and families before they leave the hospital setting.

The studies by Bentes et al (3) and Reznik et al (4), though the methodologies they use are quite different, attempt to estimate the long-term risk for developing epilepsy after a specific acute insult.

## Risk of Epilepsy After a Stroke

Stroke is recognized as the leading cause of epilepsy in the elderly (2). The incidence of seizures after an acute stroke has been reported between 2% to 8.2% (5–8). Still, there is a paucity of information regarding the risk factors that would predict the development of long-term poststroke epilepsy. Multiple risk factors have been proposed, including the severity, nature, and localization of the stroke as independent risk factors for the development of epileptic seizures. However, just as with patients in the intensive care unit, the clinical identification of seizures in the absence of EEG may mean practitioners will come up short in identifying seizures in vulnerable populations where seizures may be of an unusual presentation, subtle, or nonclinical.

Bentes et al (3) prospectively and clinically followed patients who had an acute stroke with a spot EEG within 72 hours of the stroke admission, daily during the acute hospital stay, at the time of hospital discharge, at the time of any functional decline or seizure, and at a year after the initial acute insult. With this very proactive approach they found seizures in 15.2% of patients within 1 year. Specifically, 14.6% of patients had seizures within the first week after a stroke, 2.6% were in nonconvulsive status epilepticus, and 22.7% had seizures that were seen only on EEG. These findings support the use of EEG within the week after an acute stroke as it may at least improve the practitioner's ability to diagnose poststroke epilepsy. This group also showed focal symptoms presumed to be related to stroke and that may in fact have been manifestations of epileptic seizures. Another interesting point is the fact that a third of patients who had acute symptomatic seizures went on to develop further seizures within a year of follow-up.

Given the high incidence of ischemic stroke, the possibility of predicting who will develop epilepsy and when becomes an intriguing task. It would be ideal to discuss the risk of seizures with patients before they leave the hospital after an acute vascular event and even consider the possibility of treatment when indicated. At least two clinical scales have taken a practical approach to answer this question: The post-stroke epilepsy risk scale (PoSERS) (6) scale, which includes the stroke location, subtype, persisting neurologic deficits, presence of established vascular encephalopathy, and presence of early- and late-onset seizures, showed good specificity and predictive values. The SeLECT scoring system, named thusly to reflect the included parameters of severity of stroke, large artery atherosclerotic aetiology, early seizures, cortical involvement, and territory of middle cerebral artery involvement, models these five variables to predict post-stroke seizures. The SeLECT score also showed very good performance in predicting seizures at 1 year and 5 years after a stroke. Both scales use data that are readily available to the stroke treating team in the hospital setting. Interestingly, however, EEG was not found to be a good predictor for long-term seizures in either of these scales.

Maybe we should learn lessons from studies of critically ill patients with seizures and perform more EEGs routinely in patients after stroke. Future studies will hopefully provide better information regarding this indication.

## Risk of Seizures and Epilepsy After Sepsis

Reznik et al (4) conducted a retrospective cohort study review and found an annual incidence of seizures of 1.29% in survivors of sepsis, which is about five times higher than the risk in the general population and other hospitalized patients. This increased risk was highest in patients with known neurologic involvement but also increased in patients with no neurologic deficit at the time of admission.

The presence of unrecognized EEG seizures in the critically ill patient has been well demonstrated (9, 10). This study provides evidence of the potential that sepsis may cause long-term brain injury and enduring epilepsy beyond the acute hospital stay. The specific risk factors that would make some survivors of sepsis more likely to develop epilepsy, besides a known neurologic involvement, have yet to be identified at this time. The possibility that undiagnosed seizures may contribute to long-term neurologic decline and encephalopathy is an important one to study; as is the possibility that these same risk factors contribute to the development of chronic epilepsy.

The increased risk of developing chronic epilepsy following an acute ischemic stroke or sepsis should call for the implementation of an education initiative at the time of a patient's hospital discharge. Both patients and families should receive education regarding the risk for seizures, seizure presentation, first aid, and even precautions and restrictions. Patients should know that if they experience seizures they will present relatively early within the year after hospital discharge.

The decision regarding whether to perform repeated EEGs in the absence of identified epileptic signs and symptoms is less clear, as is the need for and duration of seizure prophylaxis



in such cases. Nevertheless, making patients and clinicians aware of the increased risk of epilepsy after these conditions can facilitate a timely diagnosis and an early initiation of effective treatment before complications of undiagnosed seizures, including falls and cognitive decline, are interpreted as chronic, inevitable, consequences of the initial injury.

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